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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,856	06/29/2001	Joffre Baker	P0894P1D2C4	9045

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/896,856	Applicant(s) Baker et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 31-42 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 31-42 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Objections

1. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 38-40 have been renumbered 38-42.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 & 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application is apparent for generically treating ciliary neurons (versus embryonic chick ciliary neurons; as it relates to claims 33 & 39),

parasympathetic neurons (i.e., as it relates to claim 38), peripheral neuropathies involving ciliary neurons or parasympathetic neurons, or for treating "neurological conditions... *caused by trauma*" (i.e., as it relates to claim 40). In contrast to Applicants' assertions on page 4 of the preliminary amendment, no such basis exists on pages 3, 4, 24-25, 30, 73, 74-75 or 107-108 of the specification; thereby, constituting new matter.

3. Claims 31-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing survival of motor neurons or embryonic chick ciliary neurons with CT-1 of SEQ ID Nos: 3 or 8, does not reasonably provide enablement for any *in vivo* method for generically treating any neurodegenerative disease state or generic neuronal population with structurally uncharacterized CT-1 polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification proposes a method of treating neurological disorders in a patient with a therapeutically effective amount of cardiotrophin-1 (CT-1). However, no disclosure is provided in the specification on how to treat any neurological disorder, nor on how to assess *in vivo* administration of an effective amount of CT-1, nor how any model system containing any neural pathways reminiscent of that found *in vivo* can be effectively treated with such. Additionally, the instant specification has failed to disclose what specific neuronal populations are responsive to the CT-1 polypeptides of the instant invention, how a similar disclosed method was practiced in

the art with a different agent, or to provide even a single *in vivo* working example of the claimed method. It is noted that although the specification does list various disorders found within the nervous system, the specification fails to describe how the instant invention can be used to treat these disorders with an effective amount of any CT-1 polypeptide, in that no disease state is known or disclosed that is dysfunctional due to altered expression of CT-1. Therefore, because of the limited guidance provided by the instant specification and the paucity of working *in vivo* models to practice the scope of the current claims, it would require undue experimentation for the skilled artisan to know how to use the CT-1 polypeptide of the instant invention for generically treating/increasing survival *in vivo* of undefined neuron populations without first discovering what neuronal populations are responsive to CT-1.

Second, the name CT-1 alone (e.g., as it is defined on page 9 of the specification) encompasses any random mutation, addition, substitution, deletion, fragment or any biologically functional equivalent of any CT-1 related polypeptide; thereby, providing no structural characterization and little functional characteristics for how to make the required CT-1 polypeptides to practice the claimed method. The specification further fails to define what specific amino acids are critical for any neurotrophic-related function, especially for a factor that normally functions on cardiac tissue. In addition, the skilled artisan would reasonably expect that random mutations to any protein (i.e., as encompassed by the current claim language) would result in inactive CT-1 related protein, and therefore a method that does not work. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a

sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger then states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for "knowing how to make or use" any CT-1-related polypeptide does not in itself provide sufficient guidance on what peptides could be made which retains the desired function of the instant invention, because any such random mutation within a CT-1 polypeptide would be predicted to adversely affect the three-dimensional conformation of the polypeptide, without requiring undue experimentation to determine otherwise.

4. Claims 34 & 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Motor neurons are neurons of the CNS vs. PNS, because that is where their cell bodies reside. Therefore, it is ambiguous and confusing how treatment of a peripheral neuropathy is envisioned, as currently claimed (i.e., as it relates to claim 34).

Second, it is unclear and incomplete what the "therapeutically effective amount" is intended for, as it relates to claim 41. It is suggested that adding "for increasing neuronal survival" to claim 41 should obviate this particular rejection of claim 41.

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
August 30, 2002

PATRICIA A. DUFFY
PRIMARY EXAMINER